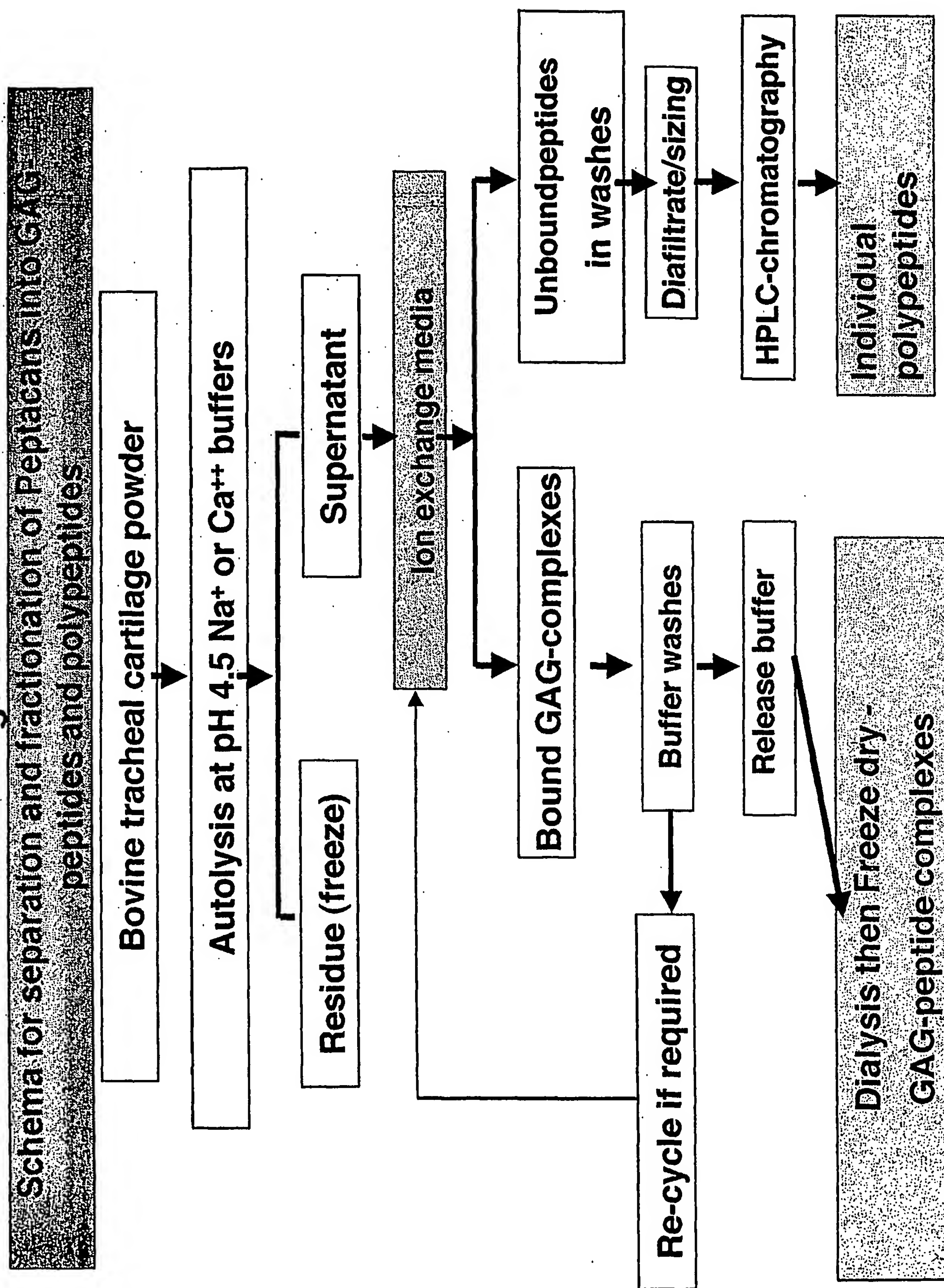
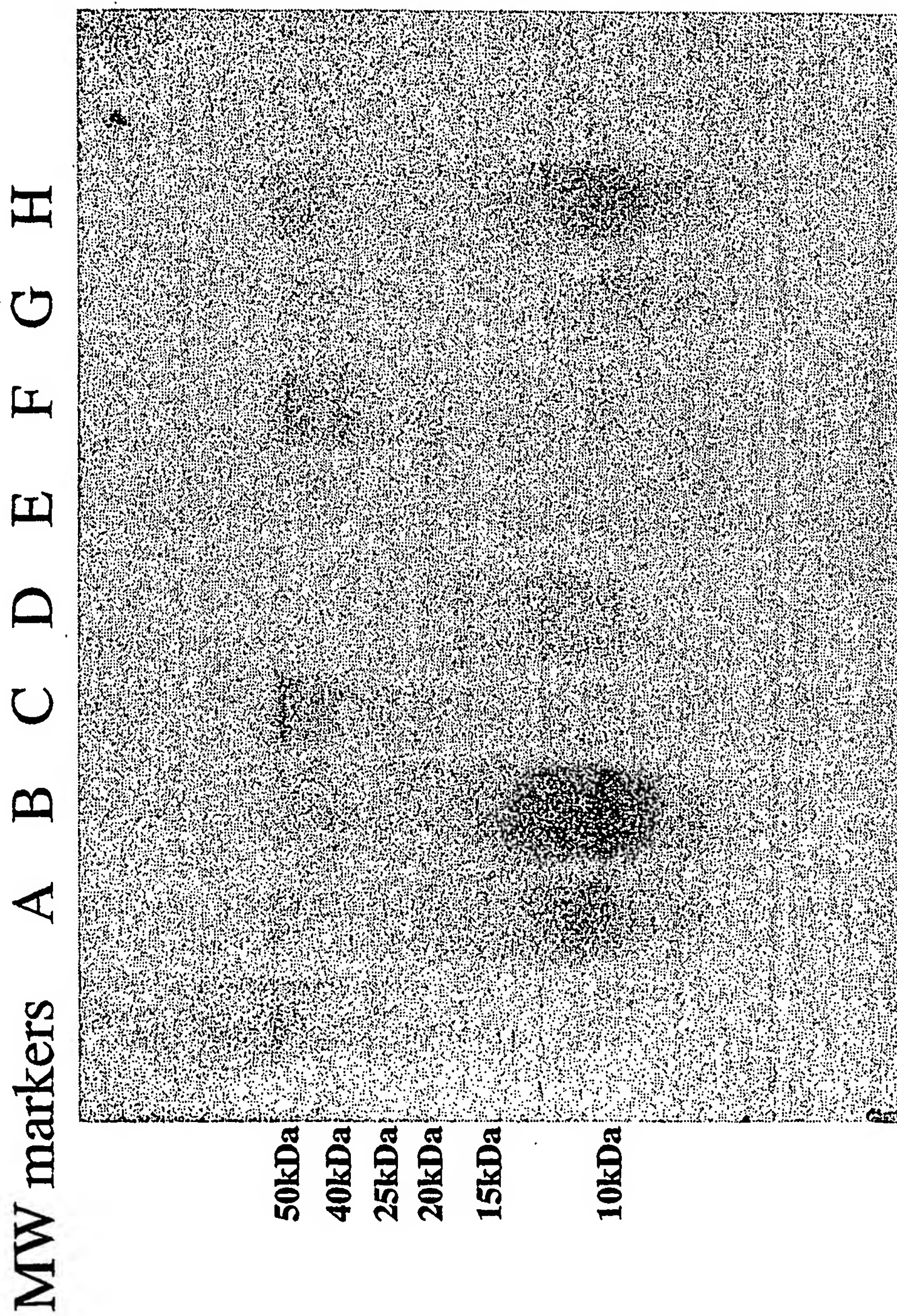


Figure 1

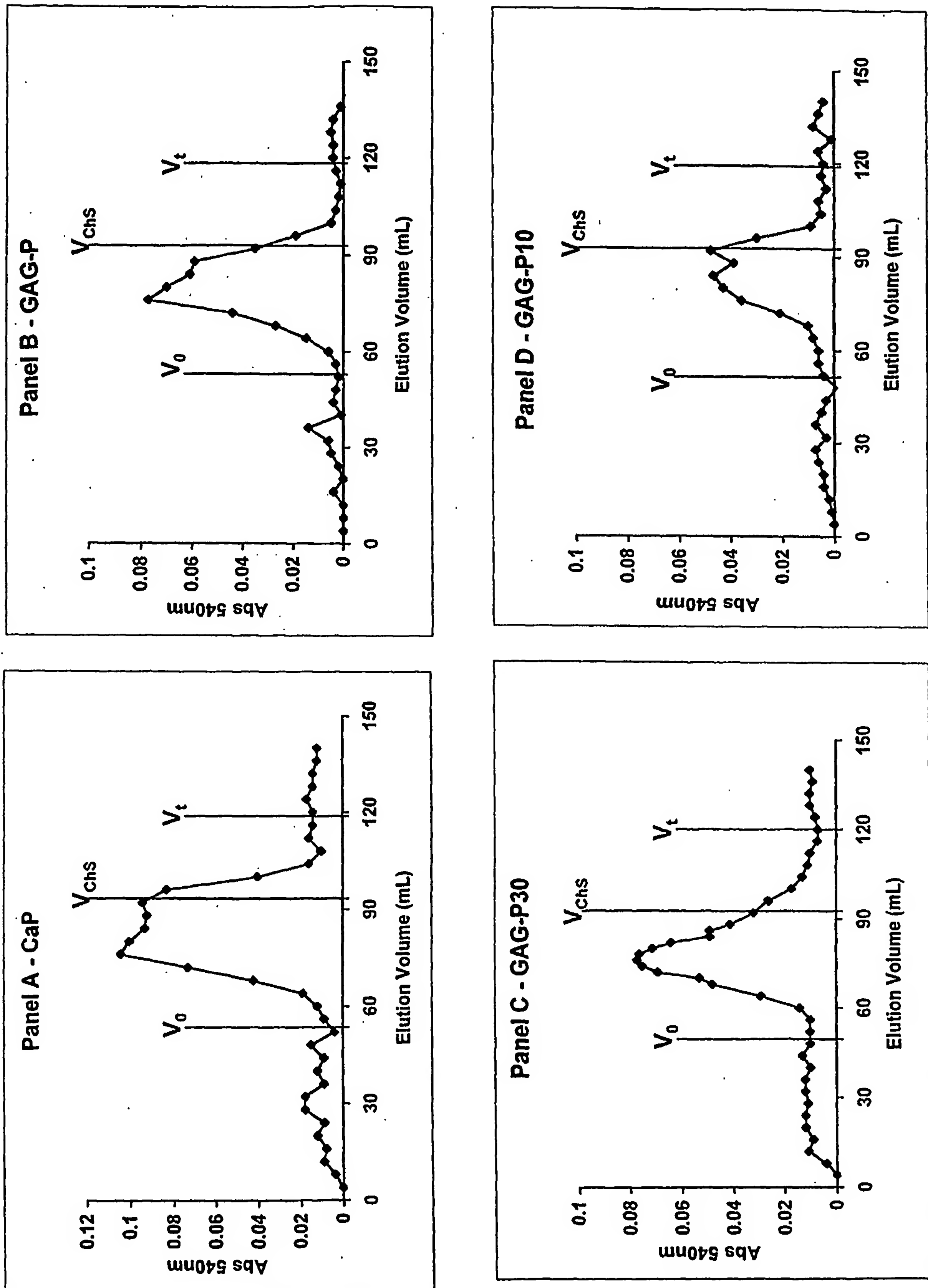


# FIGURE 2

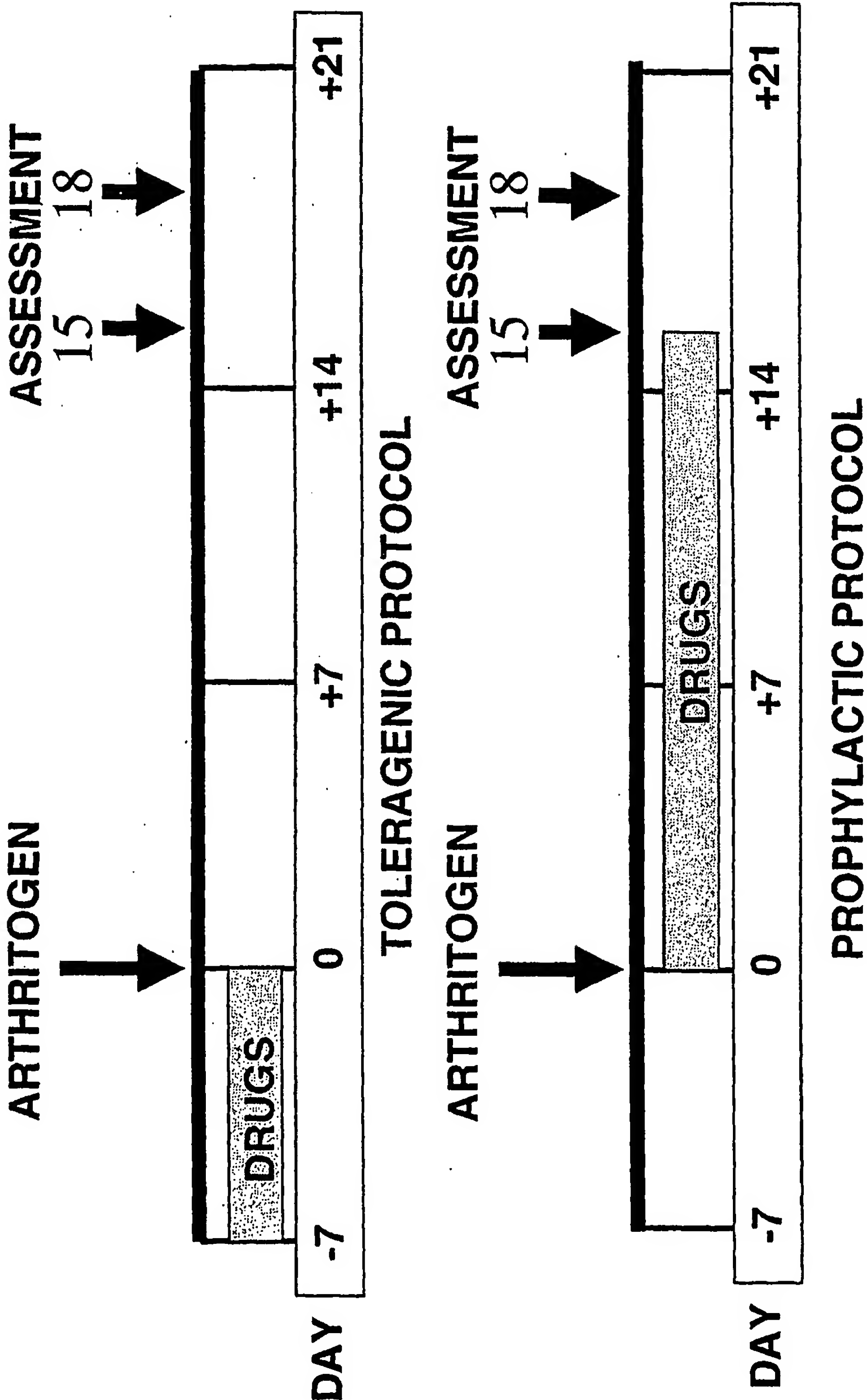




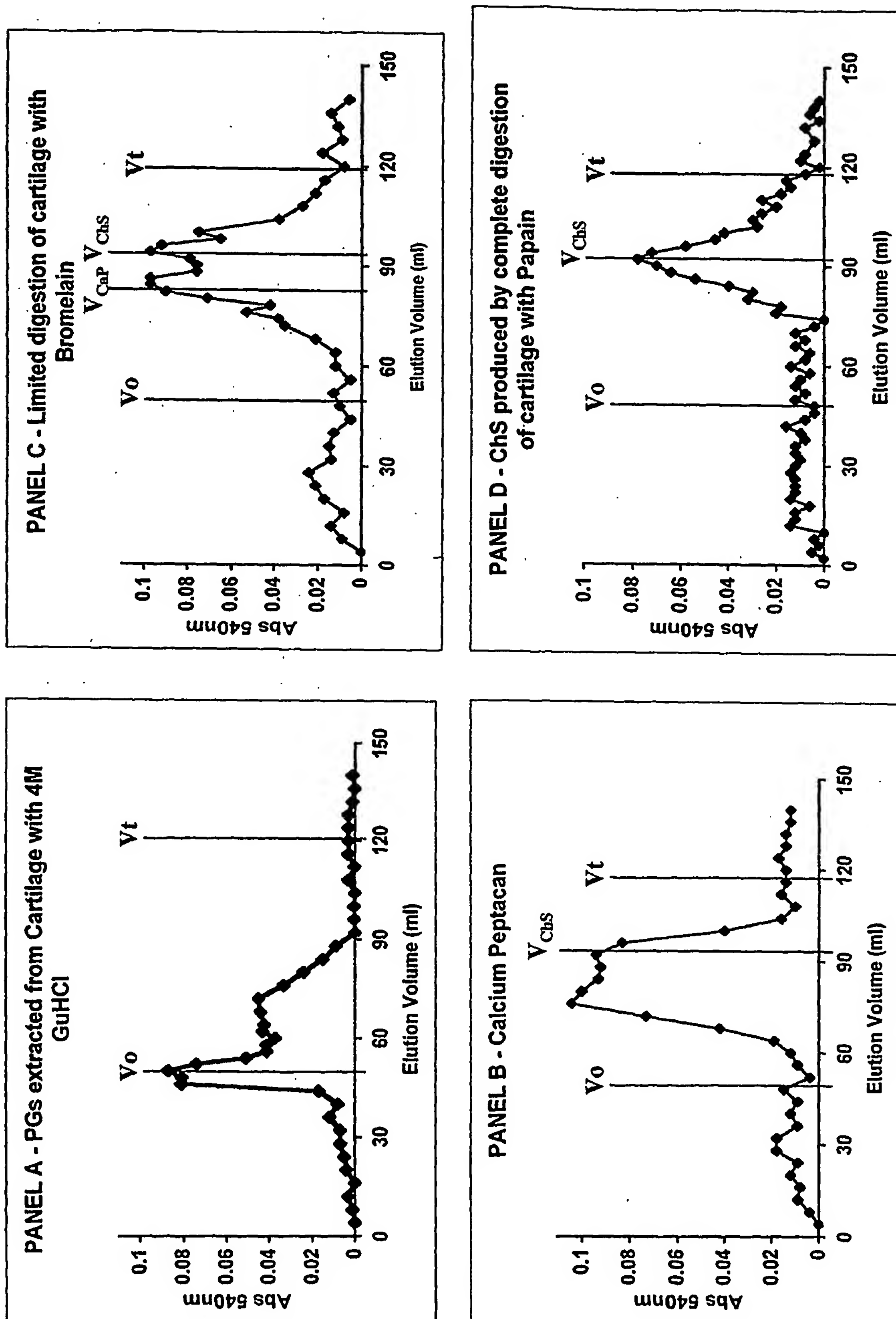
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**FIGURE 3**

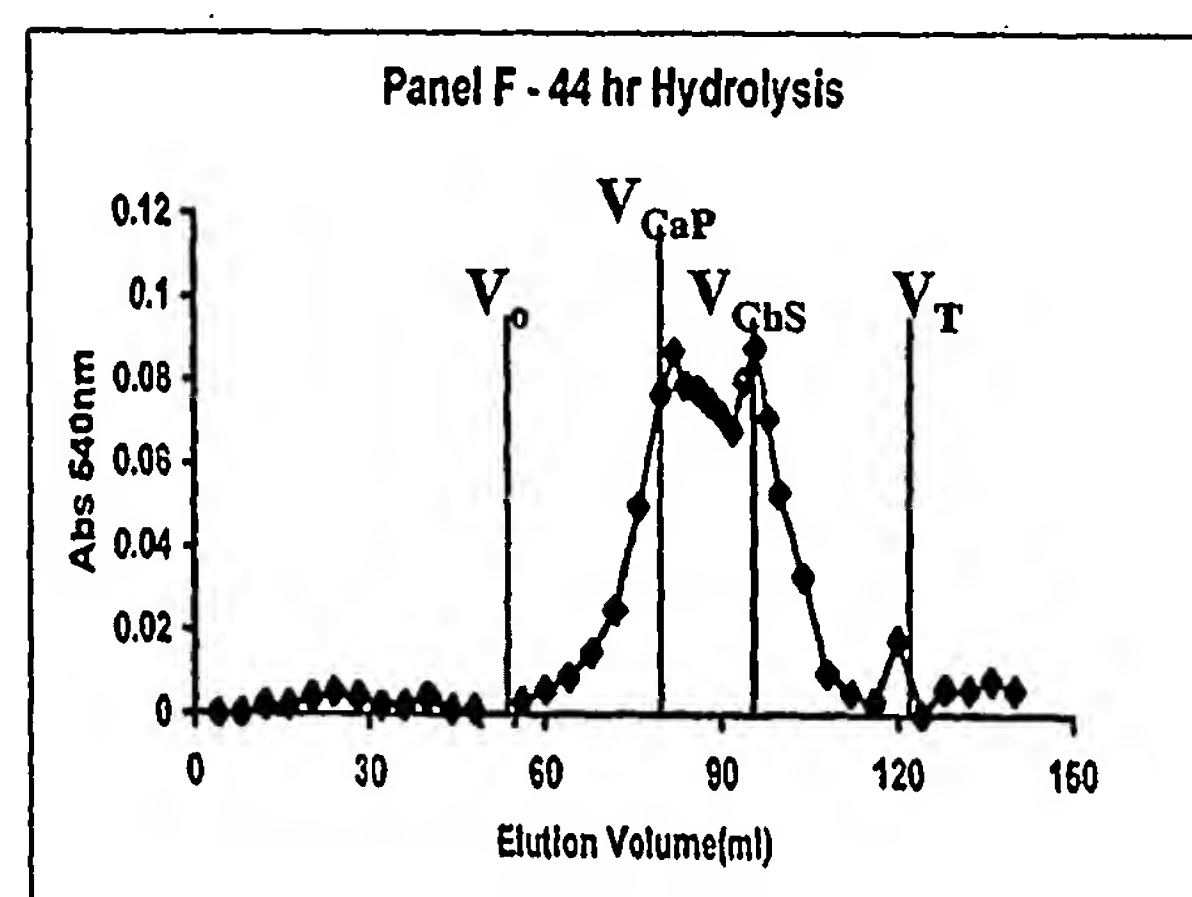
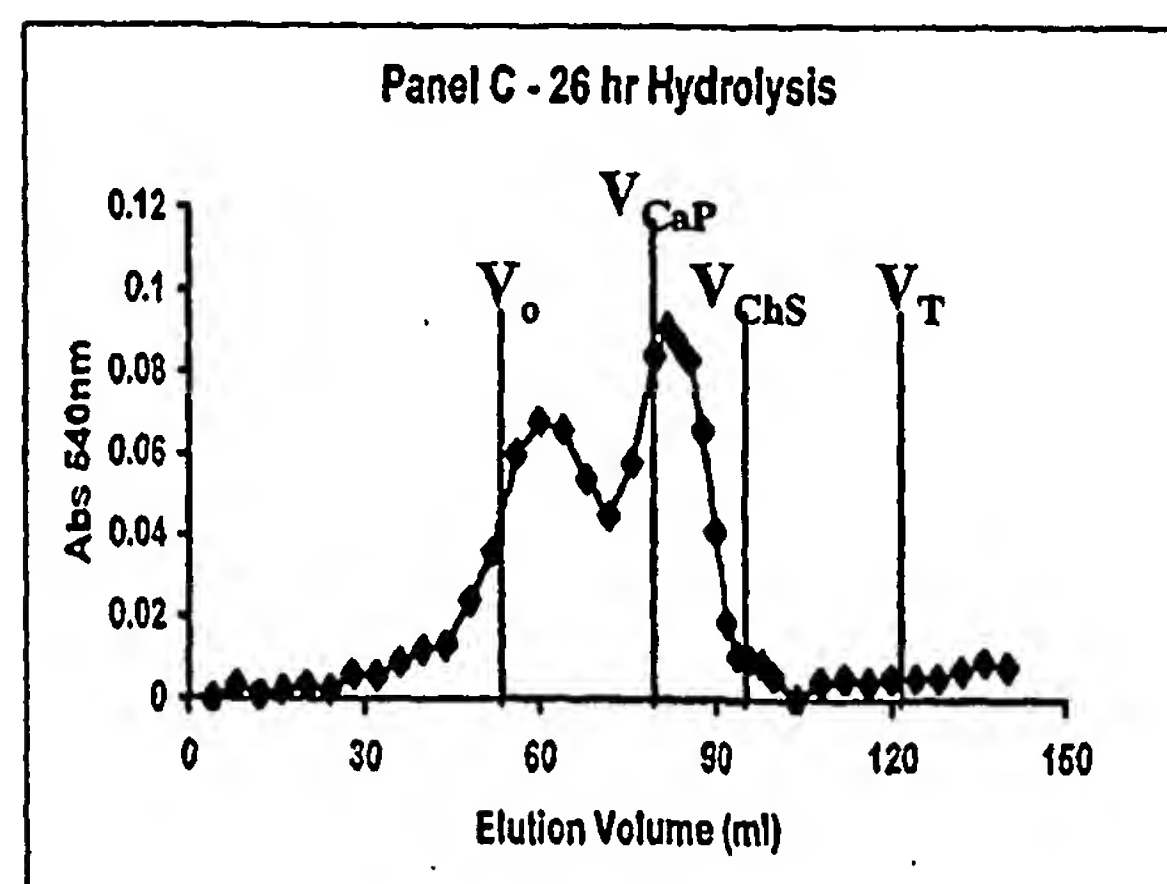
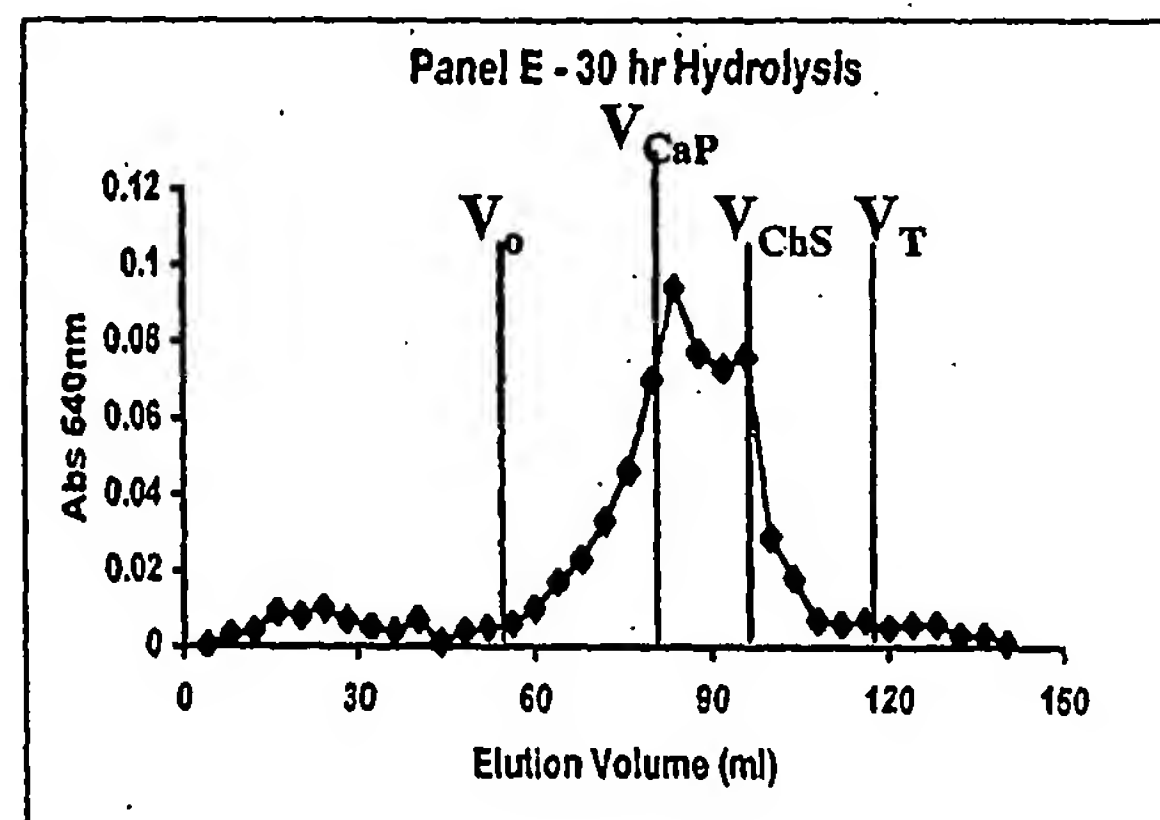
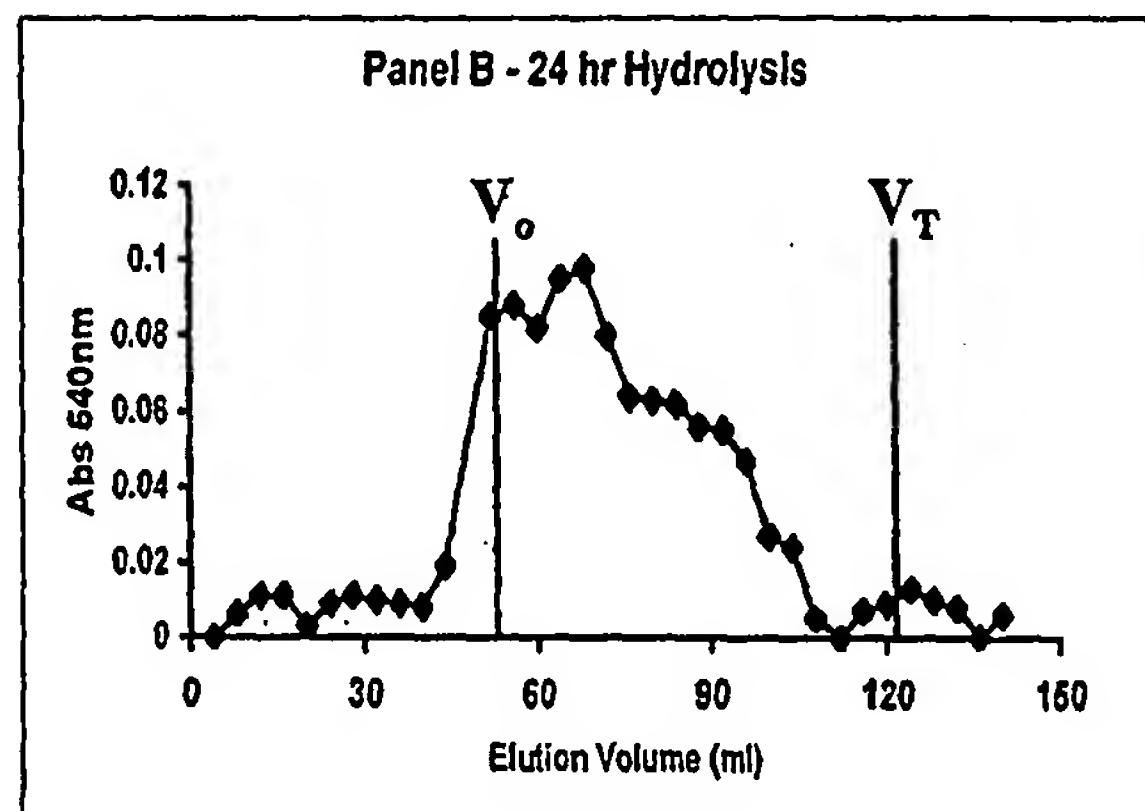
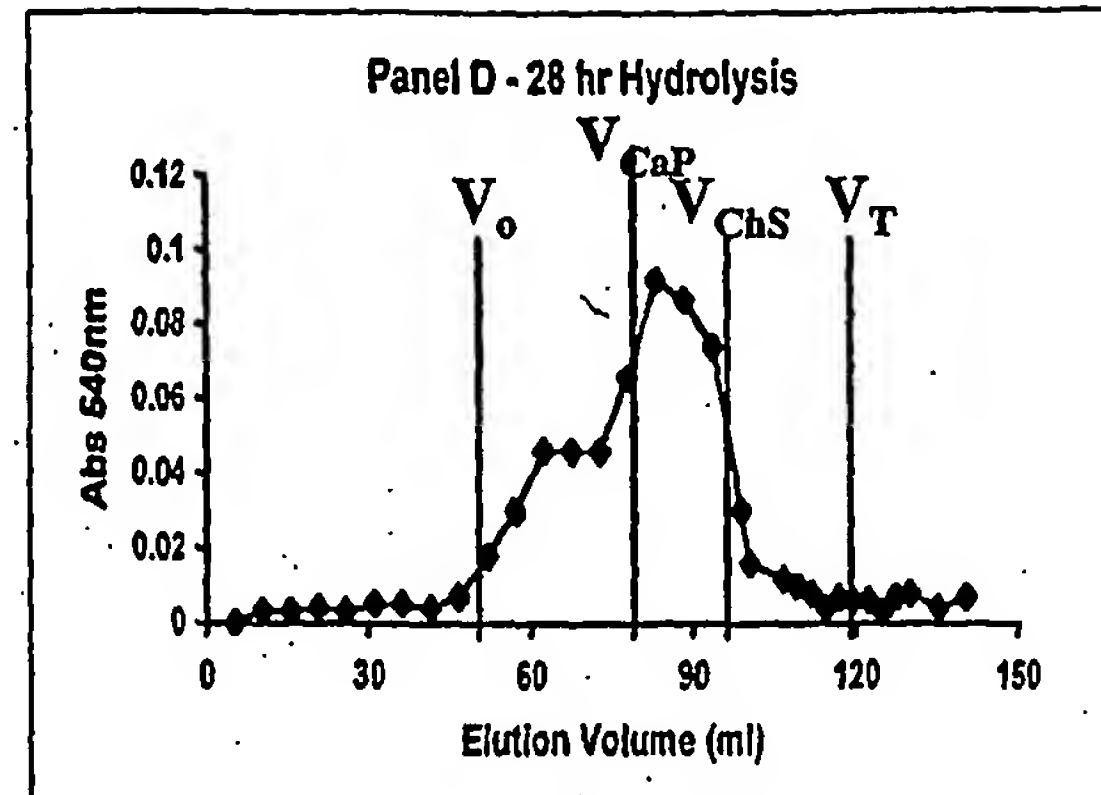
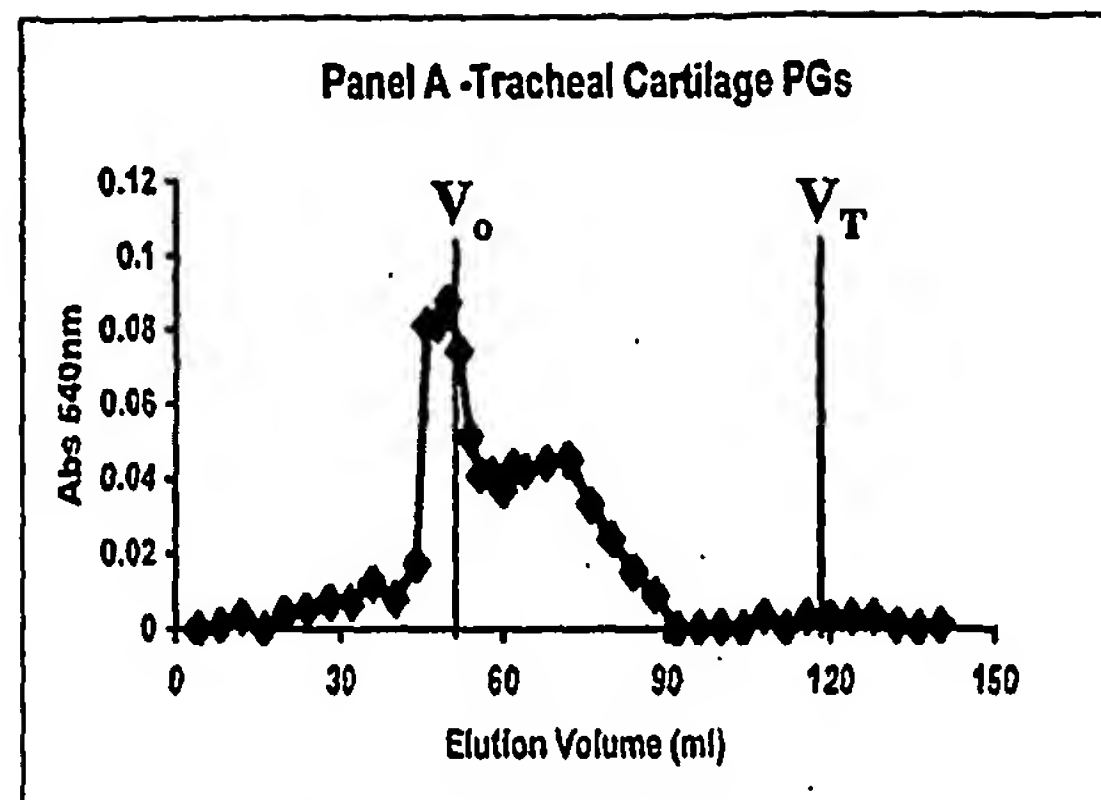
**FIGURE 4**  
**Protocols used to evaluate drugs**  
**in the rat CIA (COL-II) and AIA (*Mtb*) models**



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**FIGURE 5**

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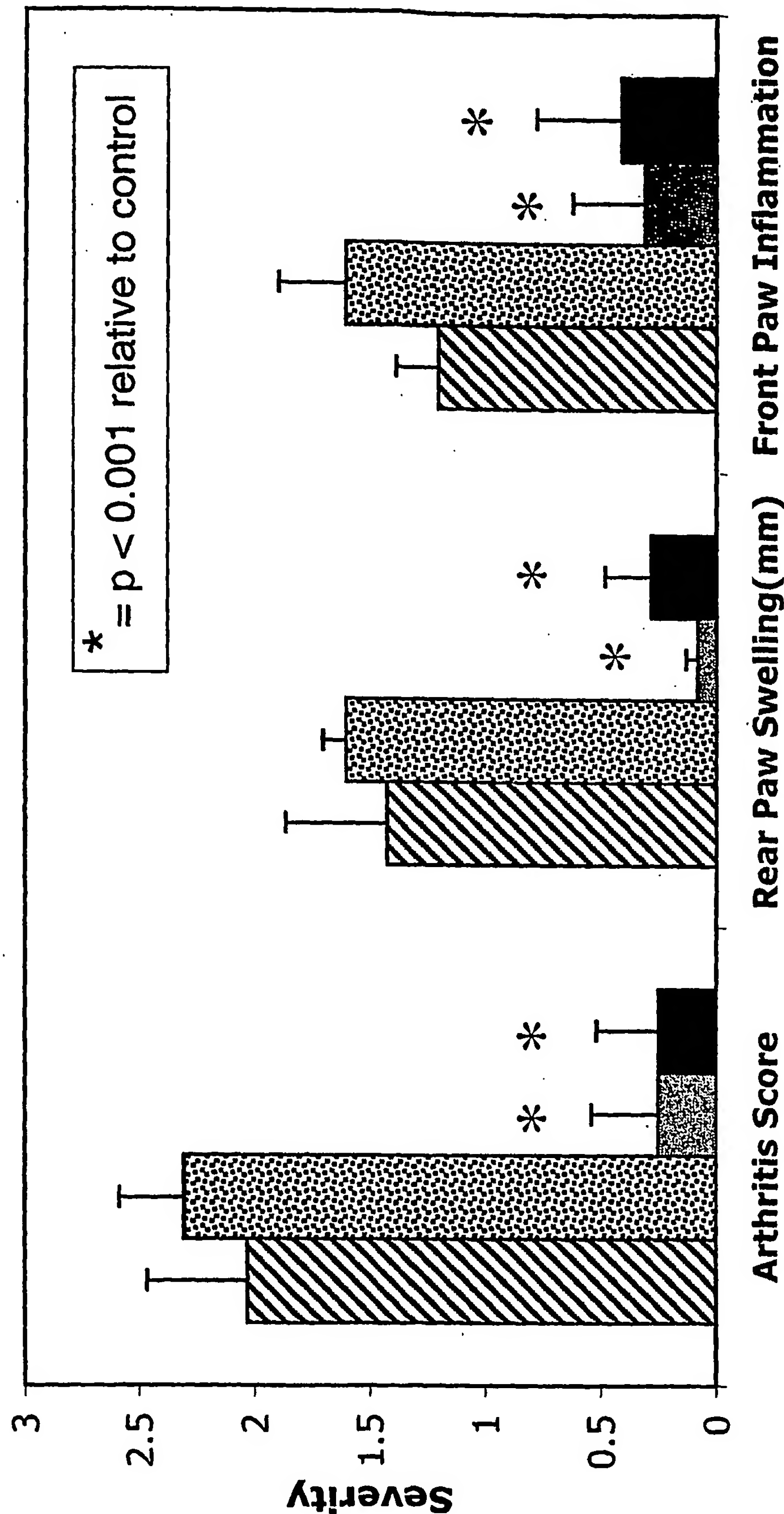
**FIGURE 6**

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# FIGURE 7

## RAT CIA TOLERAGENIC PROTOCOL DAY 15

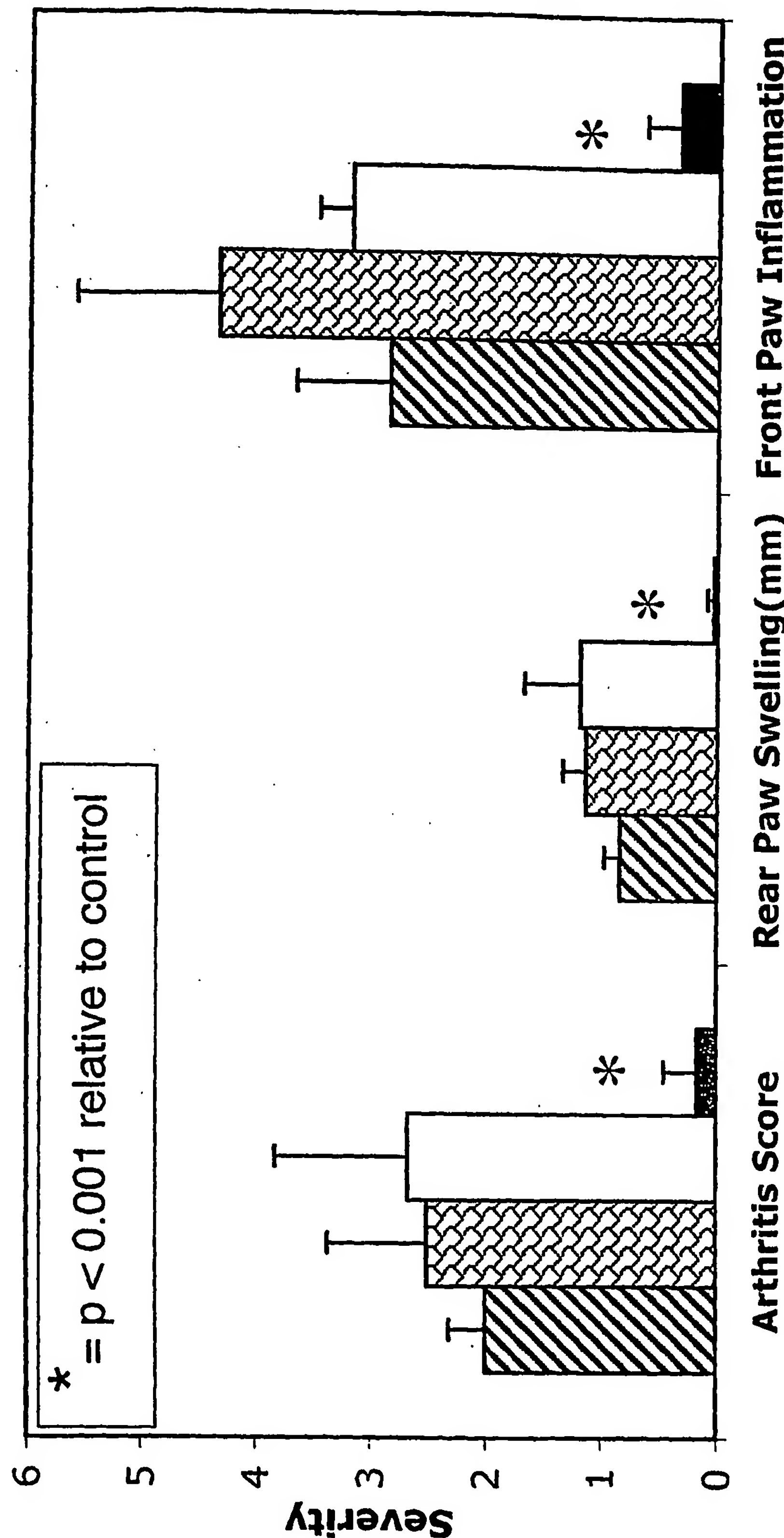
Control ChS(20mg/kg) CaP(10mg/kg) Coll-II(10mg/kg)



# FIGURE 8

## RAT CIA PROPHYLACTIC PROTOCOL DAY 15

□ Control ▨ GmSO4(200mg/kg) □ GmHCl(200mg/kg) ■ CaP(20mg/kg)



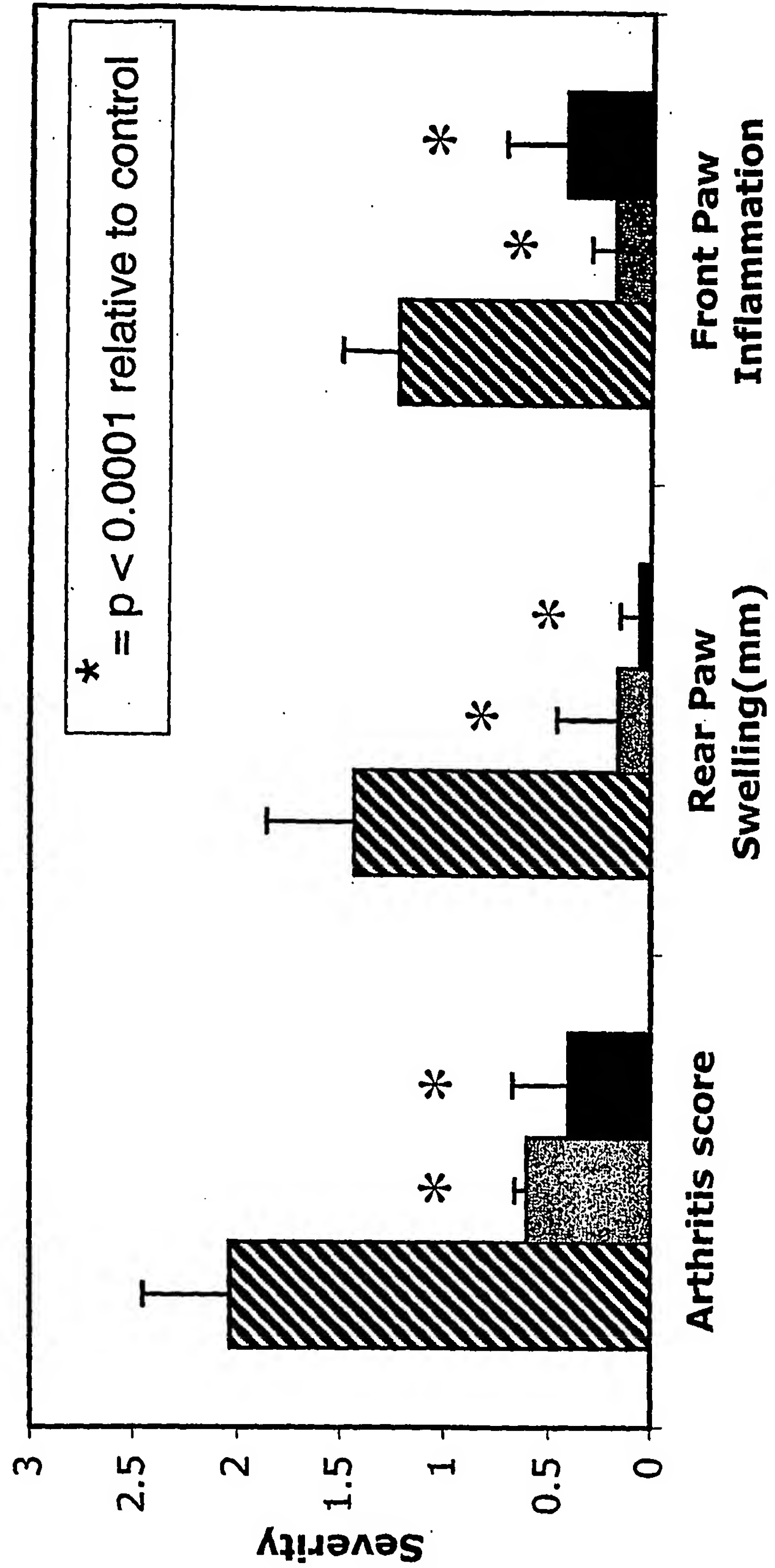


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# FIGURE 9

## RAT CIA TOLERAGENIC PROTOCOL DAY 15

▨ Controls    ▨ CaP(20mg/kg)    ■ GAG-P(20mg/kg)

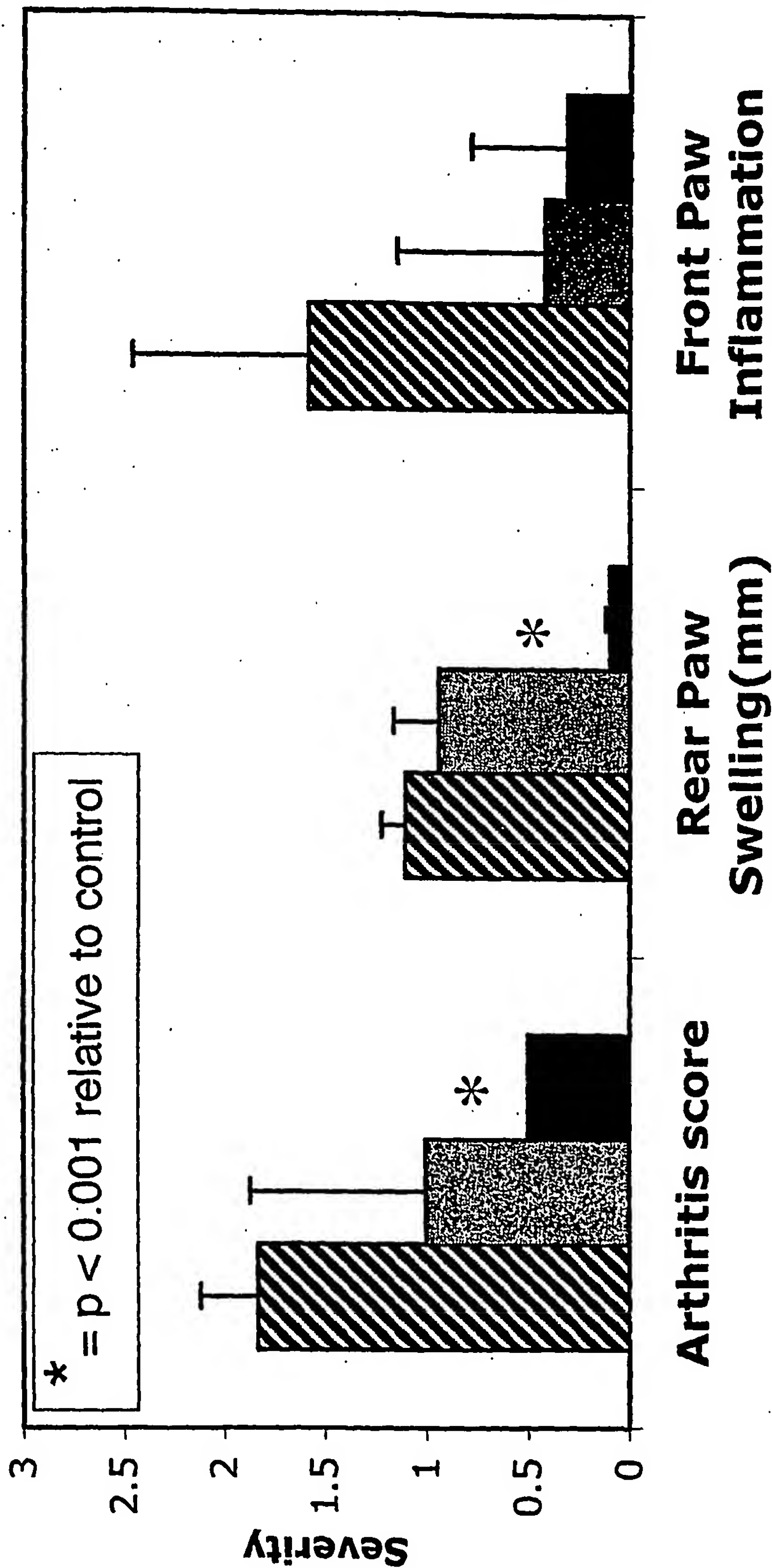


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**FIGURE 10**

**RAT CIA TOLERAGENIC PROTOCOL DAY 18**

**▨ controls ▨ CaP(20mg/kg) ▨ GAG-P(20mg/kg)**

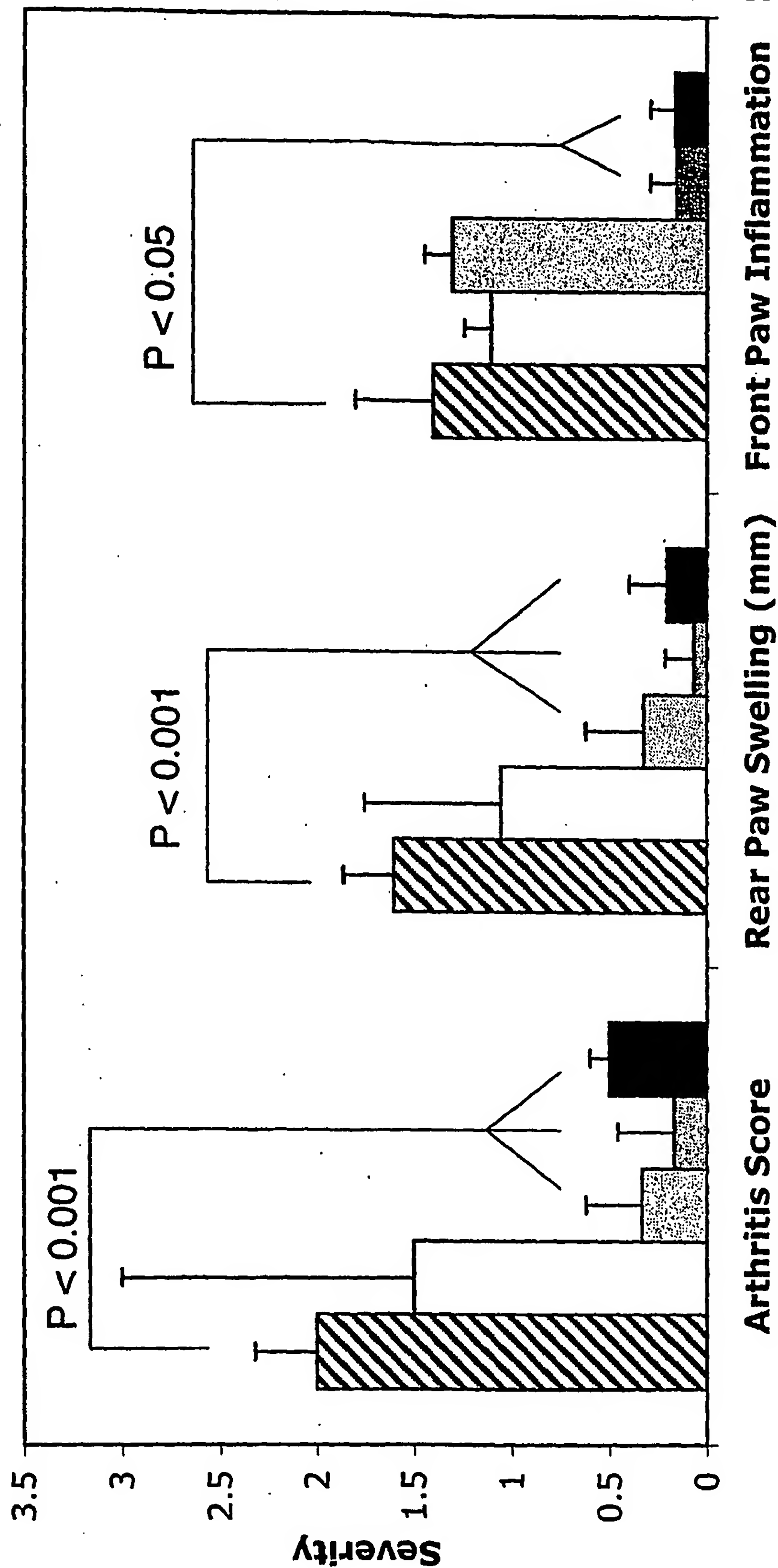


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# FIGURE 11

## RAT CIA PROPHYLACTIC PROTOCOL DAY 15

Control □ CaP(3.3mg/kg) ▨ CaP(10mg/kg) ▩ CaP(20mg/kg) ■ CaP(200mg/kg)

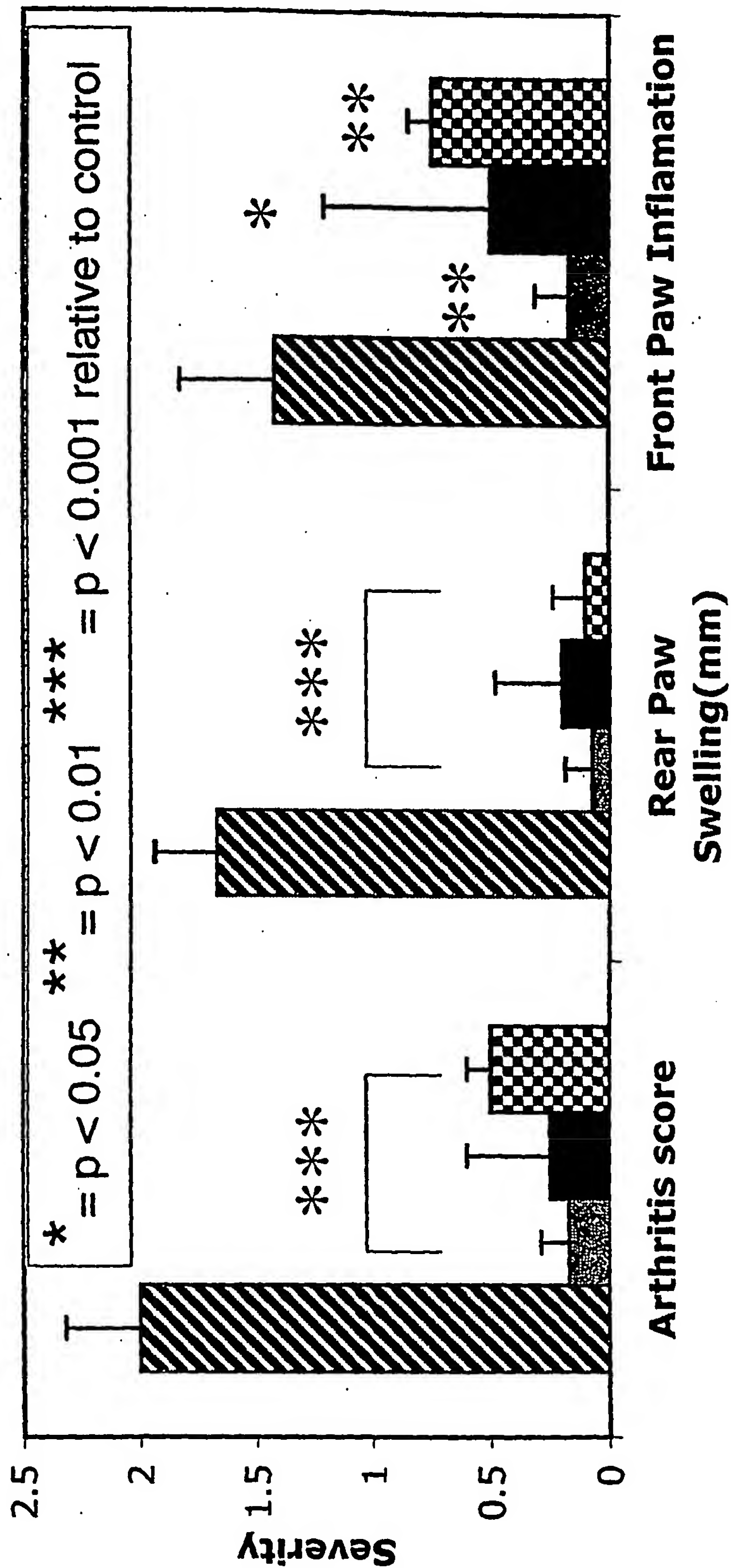


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FIGURE 12

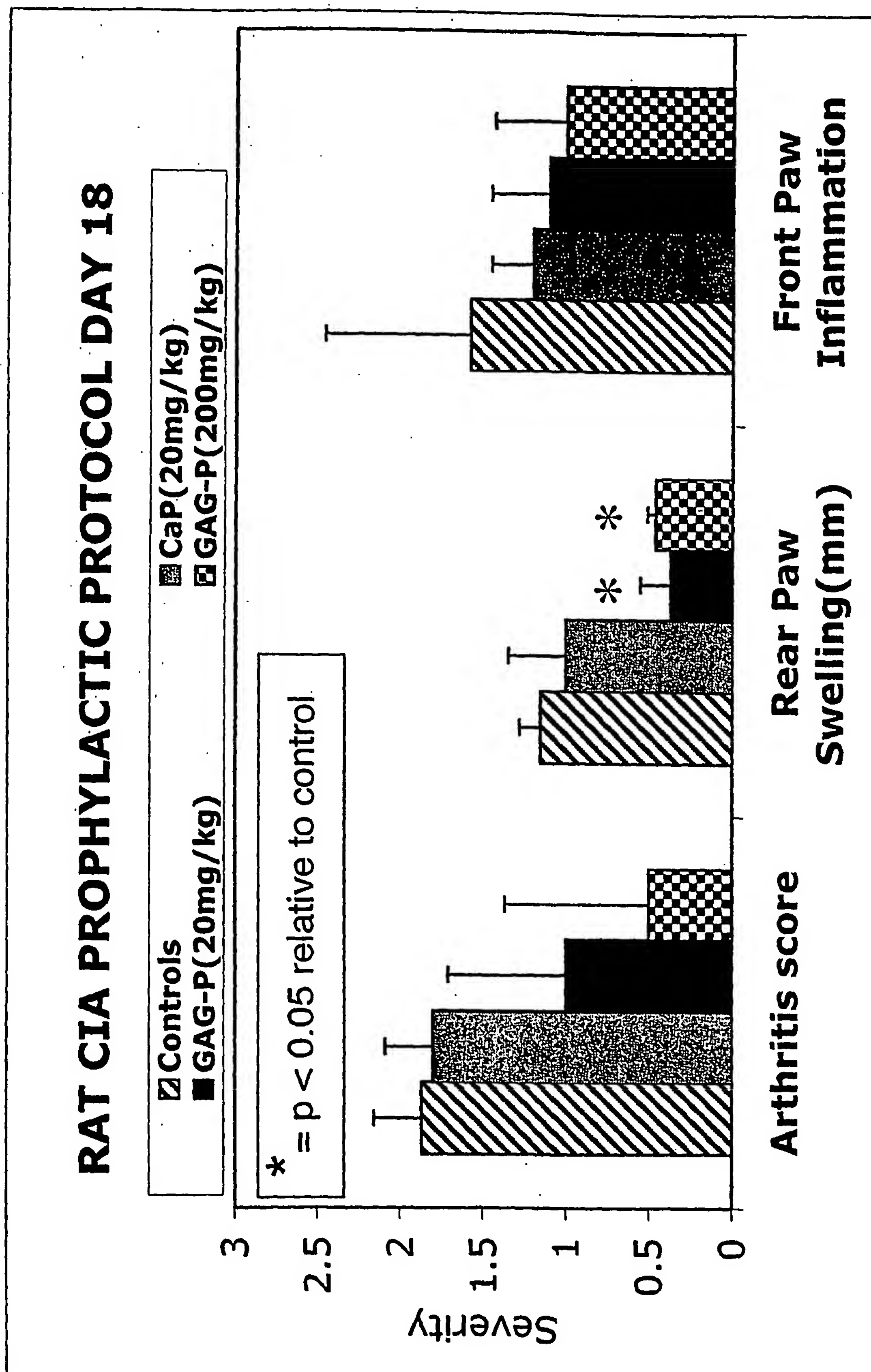
RAT CIA PROPHYLACTIC PROTOCOL DAY 15

Controls ■ CaP(20mg/kg) ■ GAG-P(20mg/kg) ■ GAG-P(200mg/kg)



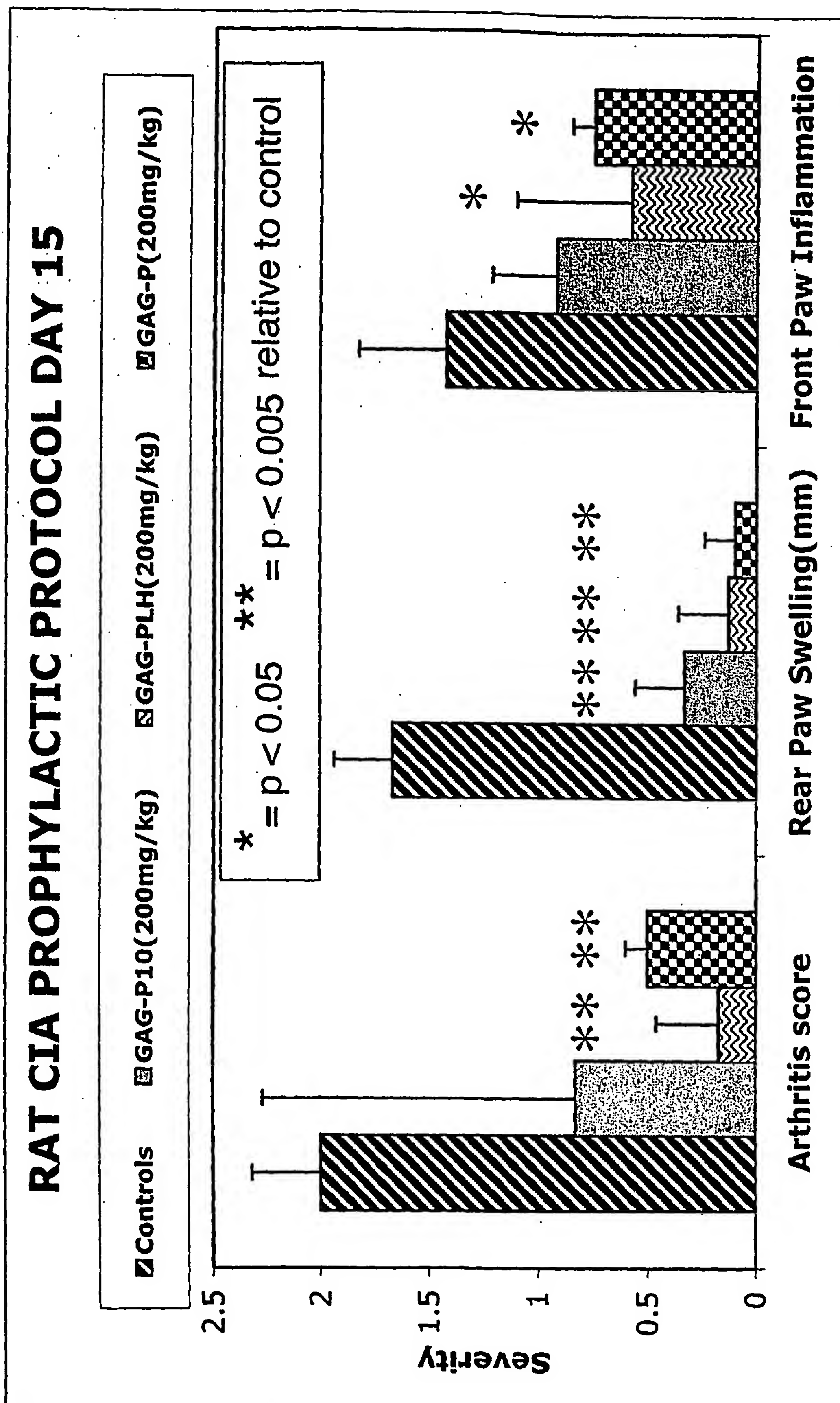


**FIGURE 13**



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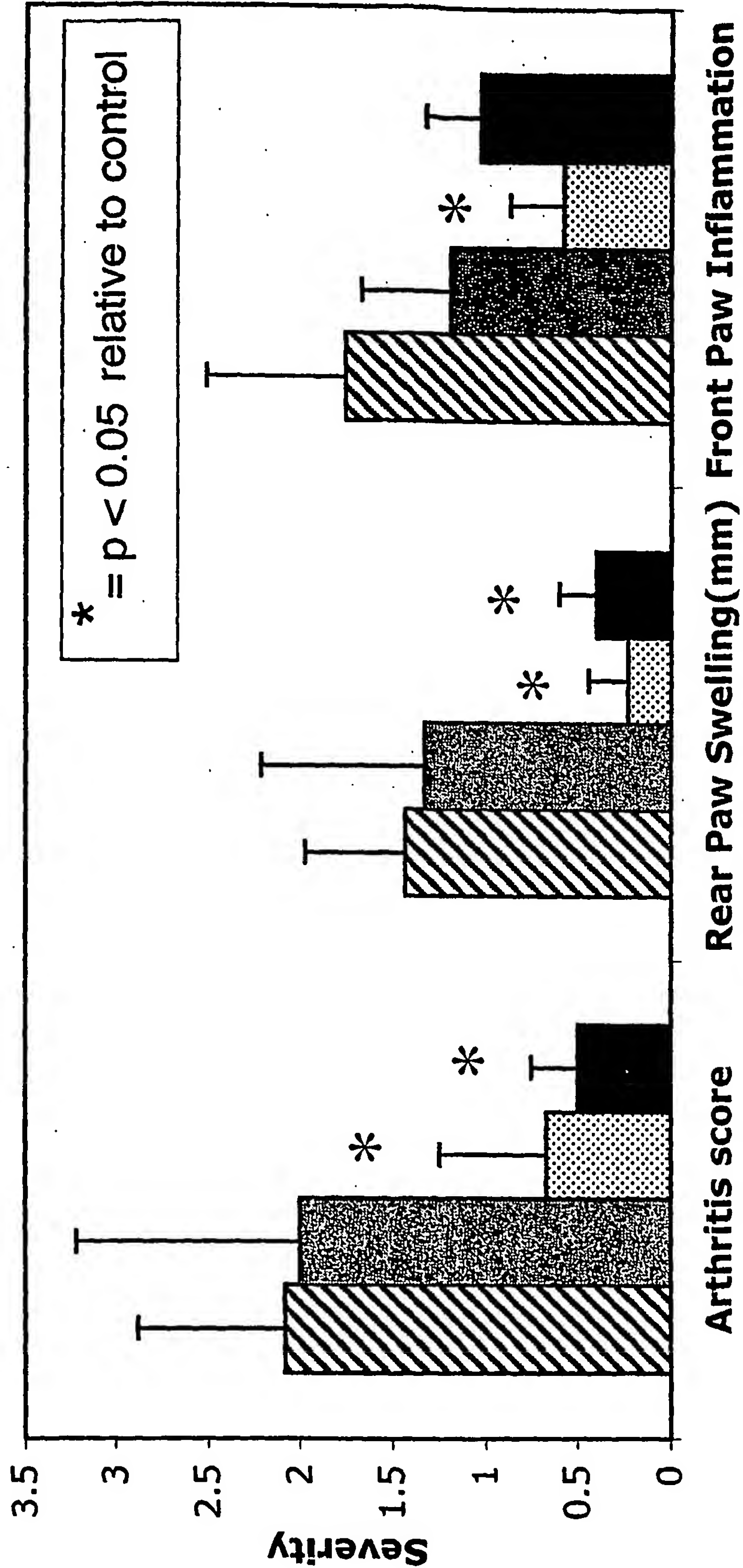
FIGURE 14



# FIGURE 15

## RAT AIA PROPHYLACTIC PROTOCOL DAY 15

▨ Controls ▨ CaP(20mg/kg) ▨ CaP(200mg/kg) ▨ GAG-P(20mg/kg)



**FIGURE 16**

**RAT AIA PROPHYLACTIC PROTOCOL DAY 18**

▨ Controls ▨ CaP(20mg/kg) ▨ CaP(200mg/kg) ■ GAG-P(20mg/kg)

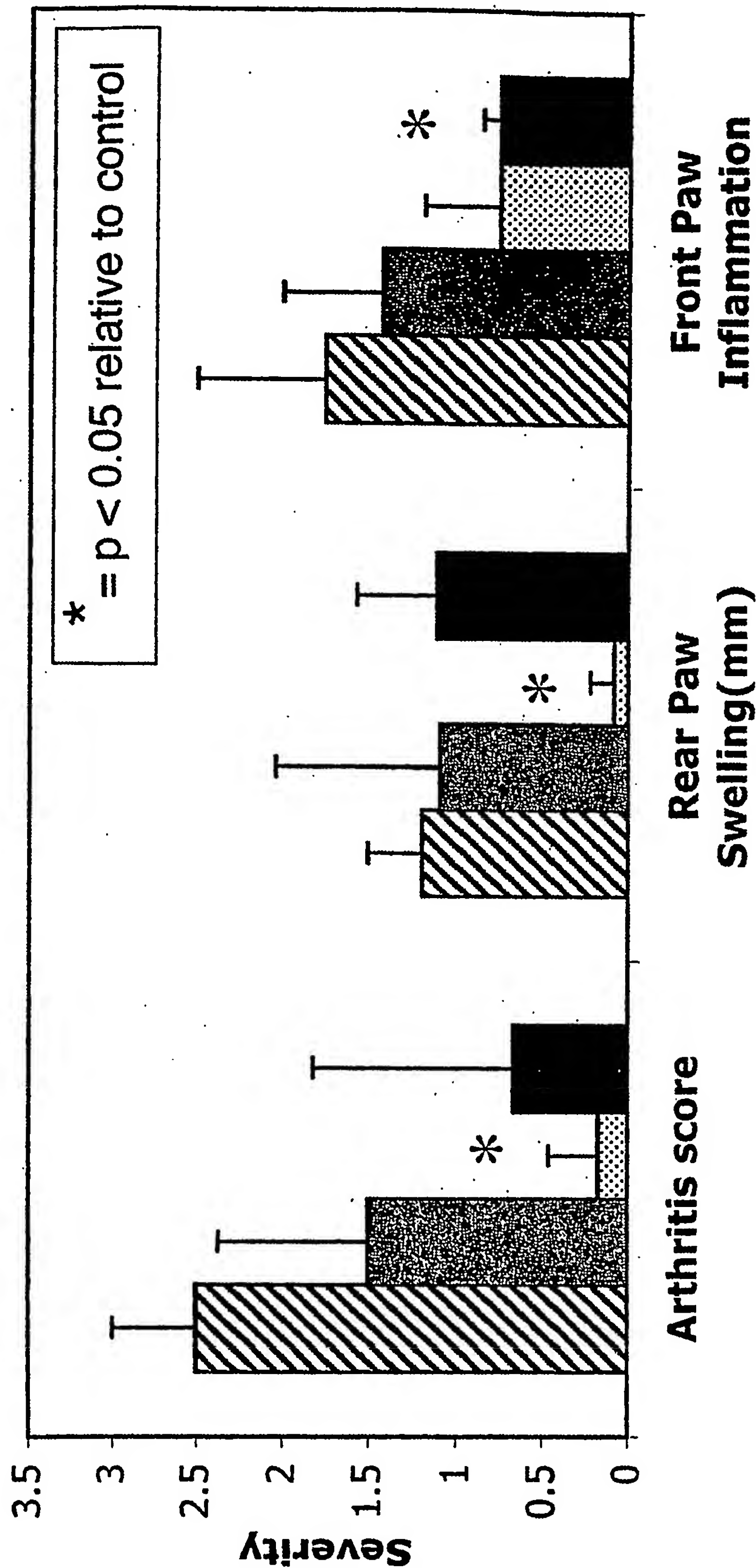
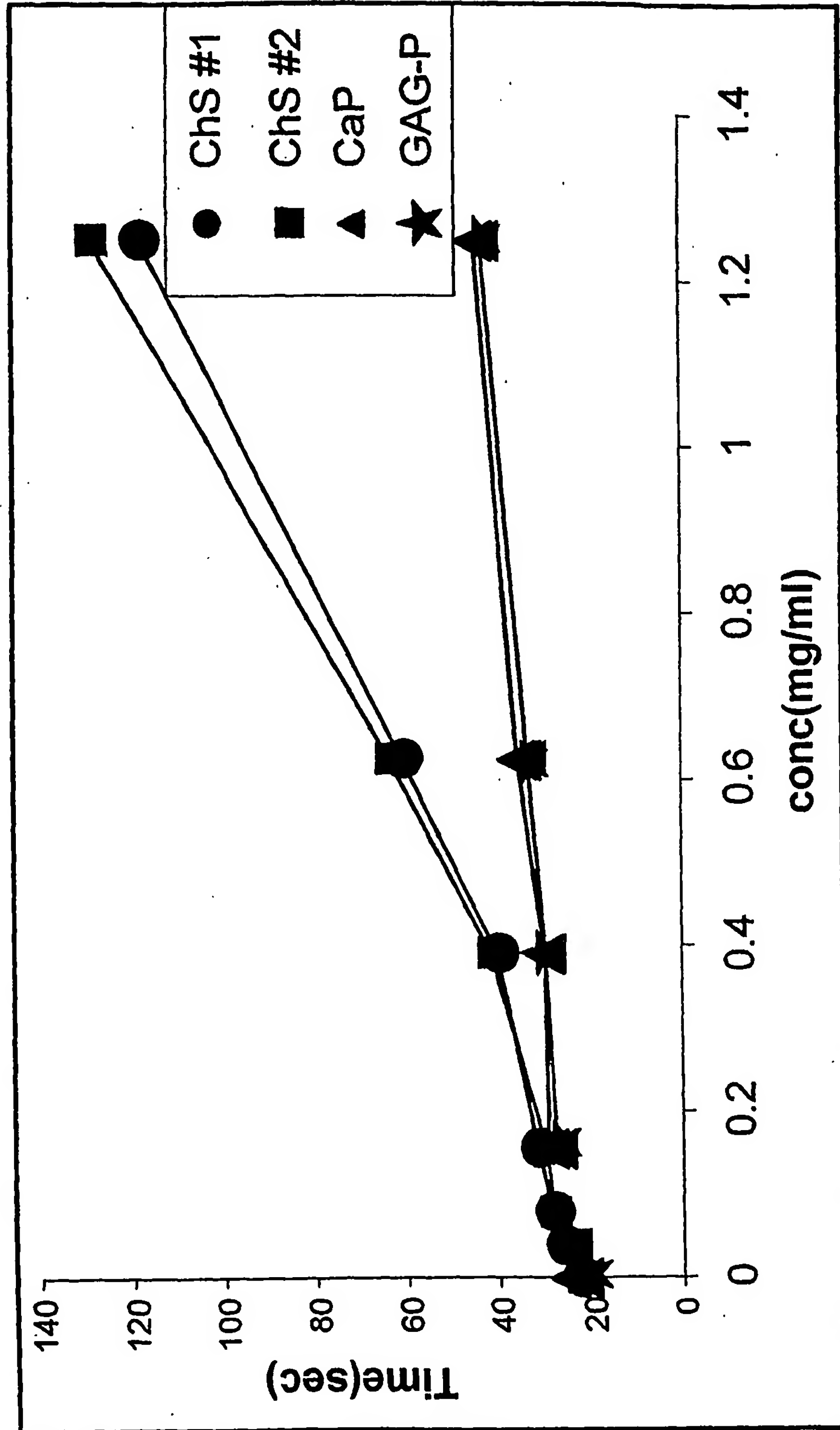




FIGURE 17



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**TABLE 1**

**Gastroprotective activity of Calcium Peptacan (CaP) in the Rat CIA Arthritis Model against haemorrhagic stomach lesions produced by oral administration of the non-steroidal anti-inflammatory drug, Ibuprofen (Nurofen<sup>®</sup>) (50 mg/kg) on day 20. In this model arthritis is manifest by day 15**

<b>Treatment</b>	<b>Period of treatment (days)</b>	<b>Mean number of lesions</b>	<b>Number of Rats</b>
Nil		25	7
CaP (20mg/kg/day, orally)	0-15	4	3
CaP (200mg/kg/day, orally)	0-15	9	3
CaP (200mg/kg/day, orally)	17-20	7	4
Aurothiomalate (6.3mg/kg, s.c.)	Days 1,3,5,7,9,11,13,15	14	2
Non-arthritic controls nil treatment	Nil	2	5

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**TABLE 2: Topical anti-inflammatory activity of Cream base with and without the addition of the Glycosaminoglycan preparation, GAG-PLH prepared by limited hydrolysis of cartilage. Decrease of Sodium Lauryl Sulfate Induced erythema determined from difference on day 1 (t=1) to day 8 (t=4). In 8 of 10 subjects Cream base + GAG-PLH showed lower scores than Cream base alone demonstrating higher anti-inflammatory activity with GAG-PLH.\***

Test Subject Nos: 7055

Left Arm	Cream Base	Right Arm	Cream Base + GAG-PLH
t=1 2 0 0 0 0 0 0 0 0	t=1 3 2 2 2 2 2 2 2 2	t=1 3 2 2 2 2 2 2 2 2	t=1 3 2 2 2 2 2 2 2 2
t=2 2 0 0 0 0 0 0 0 0	t=2 3 2 2 2 2 2 2 2 2	t=2 3 2 2 2 2 2 2 2 2	t=2 3 2 2 2 2 2 2 2 2
t=3 2 0 0 0 0 0 0 0 0	t=3 3 2 2 2 2 2 2 2 2	t=3 3 2 2 2 2 2 2 2 2	t=3 3 2 2 2 2 2 2 2 2
t=4 2 0 0 0 0 0 0 0 0	t=4 3 2 2 2 2 2 2 2 2	t=4 3 2 2 2 2 2 2 2 2	t=4 3 2 2 2 2 2 2 2 2
Mean Change: t=1 to t=4	-1.0	Mean Change: t=1 to t=4	-2.0

Test Subject Nos: 7381

Left Arm	Cream Base	Right Arm	Cream Base + GAG-PLH
t=1 2 0 0 0 0 0 0 0 0	t=1 3 2 2 2 2 2 2 2 2	t=1 3 2 2 2 2 2 2 2 2	t=1 3 2 2 2 2 2 2 2 2
t=2 2 0 0 0 0 0 0 0 0	t=2 3 2 2 2 2 2 2 2 2	t=2 3 2 2 2 2 2 2 2 2	t=2 3 2 2 2 2 2 2 2 2
t=3 2 0 0 0 0 0 0 0 0	t=3 3 2 2 2 2 2 2 2 2	t=3 3 2 2 2 2 2 2 2 2	t=3 3 2 2 2 2 2 2 2 2
t=4 2 0 0 0 0 0 0 0 0	t=4 3 2 2 2 2 2 2 2 2	t=4 3 2 2 2 2 2 2 2 2	t=4 3 2 2 2 2 2 2 2 2
Mean Change: t=1 to t=4	-1.3	Mean Change: t=1 to t=4	-1.8

Test Subject Nos: 7389

Left Arm	Cream Base + GAG-PLH	Right Arm	Cream Base
t=1 2 0 0 0 0 0 0 0 0	t=1 3 2 2 2 2 2 2 2 2	t=1 3 2 2 2 2 2 2 2 2	t=1 3 2 2 2 2 2 2 2 2
t=2 2 0 0 0 0 0 0 0 0	t=2 3 2 2 2 2 2 2 2 2	t=2 3 2 2 2 2 2 2 2 2	t=2 3 2 2 2 2 2 2 2 2
t=3 2 0 0 0 0 0 0 0 0	t=3 3 2 2 2 2 2 2 2 2	t=3 3 2 2 2 2 2 2 2 2	t=3 3 2 2 2 2 2 2 2 2
t=4 2 0 0 0 0 0 0 0 0	t=4 3 2 2 2 2 2 2 2 2	t=4 3 2 2 2 2 2 2 2 2	t=4 3 2 2 2 2 2 2 2 2
Mean Change: t=1 to t=4	-3.0	Mean Change: t=1 to t=4	-2.7

Test Subject Nos: 7463

Left Arm	Cream Base	Right Arm	Cream Base + GAG-PLH
t=1 2 0 0 0 0 0 0 0 0	t=1 3 2 2 2 2 2 2 2 2	t=1 3 2 2 2 2 2 2 2 2	t=1 3 2 2 2 2 2 2 2 2
t=2 2 0 0 0 0 0 0 0 0	t=2 3 2 2 2 2 2 2 2 2	t=2 3 2 2 2 2 2 2 2 2	t=2 3 2 2 2 2 2 2 2 2
t=3 2 0 0 0 0 0 0 0 0	t=3 3 2 2 2 2 2 2 2 2	t=3 3 2 2 2 2 2 2 2 2	t=3 3 2 2 2 2 2 2 2 2
t=4 2 0 0 0 0 0 0 0 0	t=4 3 2 2 2 2 2 2 2 2	t=4 3 2 2 2 2 2 2 2 2	t=4 3 2 2 2 2 2 2 2 2
Mean Change: t=1 to t=4	-3.0	Mean Change: t=1 to t=4	-3.5

TABLE 2 Continued

Test Subject No: 173

Cream Base + GAG-PLH		Cream Base	
Left Arm:		Right Arm:	
t=1	2	t=1	2
t=2	2	t=2	2
t=3	1	t=3	1
t=4	0	t=4	0
Mean Change: t=1 to t=4	-3.3	Mean Change: t=1 to t=4	-2.8

Test Subject No: 180

Cream Base + GAG-PLH		Cream Base	
Left Arm:		Right Arm:	
t=1	3	t=1	2
t=2	3	t=2	2
t=3	3	t=3	1
t=4	1	t=4	-1
Mean Change: t=1 to t=4	-2.3	Mean Change: t=1 to t=4	-2.3

Test Subject No: 336

Cream Base + GAG-PLH		Cream Base + GAG-PLH	
Left Arm:		Right Arm:	
t=1	2	t=1	2
t=2	2	t=2	2
t=3	2	t=3	2
t=4	0	t=4	0
Mean Change: t=1 to t=4	-2	Mean Change: t=1 to t=4	-2

Test Subject No: 328

Cream Base + GAG-PLH		Cream Base + GAG-PLH	
Left Arm:		Right Arm:	
t=1	4	t=1	4
t=2	2	t=2	2
t=3	0	t=3	0
t=4	0	t=4	0
Mean Change: t=1 to t=4	-4	Mean Change: t=1 to t=4	-4



TABLE 2 Continued

Test Subject No: 320

Left Arm					Cream Base + GAG-PLH					Right Arm					Cream Base				
t=1	0	0	0	0	0	0	0	0	0	t=1	0	0	0	0	0	0	0	0	0
t=2	0	0	0	0	0	0	0	0	0	t=2	0	0	0	0	0	0	0	0	0
t=3	0	0	0	0	0	0	0	0	0	t=3	0	0	0	0	0	0	0	0	0
t=4	0	0	0	0	0	0	0	0	0	t=4	0	0	0	0	0	0	0	0	0
Mean Change: t=1 to t=4: -4.3					Mean Change: t=1 to t=4: -4.3					Mean Change: t=1 to t=4: -4.3					Mean Change: t=1 to t=4: -4.3				

Test Subject No: 327

Left Arm					Cream Base					Right Arm					Cream Base + GAG-PLH				
t=1	0	0	0	0	0	0	0	0	0	t=1	0	0	0	0	0	0	0	0	0
t=2	0	0	0	0	0	0	0	0	0	t=2	0	0	0	0	0	0	0	0	0
t=3	0	0	0	0	0	0	0	0	0	t=3	0	0	0	0	0	0	0	0	0
t=4	0	0	0	0	0	0	0	0	0	t=4	0	0	0	0	0	0	0	0	0
Mean Change: t=1 to t=4: -3.0					Mean Change: t=1 to t=4: -3.0					Mean Change: t=1 to t=4: -3.8					Mean Change: t=1 to t=4: -3.8				

\*ERYTHEMA SCORING SYSTEM

One hour after removal of all patches and before application of the topical medications all sites were evaluated for response using the scoring and corresponding numerical value shown below:

SCORE	VALUE
0 = no evidence of an effect	0
? = query	1
+1 = minimal, faint, uniform or spotty erythema	2
1 = pink uniform erythema covering most or all of the contact site	3
2 = pink-red erythema visibly uniform over entire contact site	4
3 = bright red erythema with or without petechias or papules	5
4 = deep red erythema with or without vesiculation or weeping	6

The same evaluation was completed at each subsequent time point (t), that is 2, 4, and 8 days after initial application on day 1.